Clinical Infectious Diseases

MAJOR ARTICLE

Pneumococcal Community-Acquired Pneumonia Detected by Serotype-Specific Urinary Antigen Detection Assays

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Background. *Streptococcus pneumoniae* is considered the leading bacterial cause of pneumonia in adults. Yet, it was not commonly detected by traditional culture-based and conventional urinary testing in a recent multicenter etiology study of adults hospitalized with community-acquired pneumonia (CAP). We used novel serotype-specific urinary antigen detection (SSUAD) assays to determine whether pneumococcal cases were missed by traditional testing.

Methods. We studied adult patients hospitalized with CAP at 5 hospitals in Chicago and Nashville (2010–2012) and enrolled in the Etiology of Pneumonia in the Community (EPIC) study. Traditional diagnostic testing included blood and sputum cultures and conventional urine antigen detection (ie, BinaxNOW). We applied SSUAD assays that target serotypes included in the 13-valent pneumococcal conjugate vaccine (PCV13) to stored residual urine specimens.

Results. Among 1736 patients with SSUAD and ≥1 traditional pneumococcal test performed, we identified 169 (9.7%) cases of pneumococcal CAP. Traditional tests identified 93 (5.4%) and SSUAD identified 76 (4.4%) additional cases. Among 14 PCV13-serotype cases identified by culture, SSUAD correctly identified the same serotype in all of them. Cases identified by SSUAD vs traditional tests were similar in most demographic and clinical characteristics, although disease severity and procalcitonin concentration were highest among those with positive blood cultures. The proportion of pneumonia cases caused by serotypes exclusively covered by PCV13 was not significantly different between the first and second July–June study periods (6.4% vs 4.0%).

Conclusions. Although restricted to the detection of only 13 serotypes, SSUAD testing substantially increased the detection of pneumococcal pneumonia among adults hospitalized with CAP.

Keywords. pneumonia; etiology; *Streptococcus pneumoniae*; adults.

Using traditional culture-based and conventional urinary antigen detection tests, the Centers for Disease Control and Prevention (CDC)–sponsored multicenter Etiology of Pneumonia in the Community (EPIC) study detected *Streptococcus pneumoniae* infrequently (~5%) among adults hospitalized with community-acquired pneumonia (CAP) [1]. The majority of pneumococcal cases in the EPIC study were detected by conventional urinary antigen detection (ie, BinaxNOW). The infrequent detection of pneumococcus in the EPIC study, and other studies, has been attributed in part to the limited sensitivity of traditional pneumococcal testing methods, recent antibiotic use, difficulty in obtaining high-quality sputum or other lower respiratory tract specimens, and delays in processing specimens for culture [1–6].

Novel serotype-specific urinary antigen detection (SSUAD) assays were recently developed by Pfizer in support of the Community-Acquired Pneumonia Immunization Trial in Adults (CAPiTA) vaccine efficacy trial [7–9]. SSUAD assays are based on the ability of individual serotype-specific monoclonal antibodies to detect the polysaccharides of the 13 serotypes covered by the 13-valent pneumococcal conjugate vaccine (PCV13) in urine. Detection of serotype-specific polysaccharides is determined by defined positivity cutoff limits. Thus, these are validated limit assays. These assays demonstrated higher sensitivity than culture or BinaxNOW urinary antigen detection and excellent specificity in a convenience sample obtained from 776 patients with radiographically confirmed CAP [9], and in a separate prospective study of adults with radiographically confirmed pneumonia [10]. Currently, SSUAD assays are only available for research purposes [7–9].

Determining serotype distribution among patients with pneumococcal pneumonia has important public health implications. Previous studies have demonstrated that vaccination of children with pneumococcal conjugate vaccines (7-valent PCV [PCV7] or PCV13) reduced the incidence of pneumococcal

Received 8 October 2017; editorial decision 20 November 2017; accepted 29 November 2017; published online January 12, 2018.

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Clinical Infectious Diseases® 2018;66(10):1504–10

DOI: 10.1093/cid/cix1066

diseases, including CAP, due to vaccine serotypes among unvaccinated adults through indirect protection [11–16]. The EPIC study was conducted in 2010–2012, bridging the transition from routine vaccination of young US children using PCV7 to PCV13 (2010) [17] and providing an opportunity to explore early changes in the burden of CAP due to the 6 new serotypes covered by PCV13. Data on the burden of pneumonia caused by PCV13 serotypes are also needed to inform recommendations for vaccination of adults with PCV13 [18].

To test the hypothesis that pneumococcal pneumonia cases were missed by traditional testing among adults enrolled in the EPIC study, we performed SSUAD assays on stored residual urine specimens from adult patients enrolled in the EPIC study. We also determined the extent to which serotypes in PCV7 still caused CAP in adults, and explored potential early changes in the proportion of pneumonia caused by the new serotypes covered by the PCV13 childhood vaccination program.

METHODS

The EPIC study enrolled adults (≥18 years old) hospitalized with clinical and radiographically confirmed pneumonia at 5 tertiary care hospitals in Chicago, Illinois and Nashville, Tennessee and has been previously described [1]. In brief, data on patient and illness characteristics and clinical care were collected using standardized questionnaires. Specimens for blood cultures and BinaxNOW pneumococcal urinary antigen detection tests were obtained and tests performed as part of the study protocol. Bacterial cultures from sputum specimens were performed for patients who were actively expectorating. Other respiratory specimens obtained for clinical care, including endotracheal aspirate, bronchoalveolar lavage, and pleural fluid specimens, were also collected and cultured, as available. Only bacterial cultures of sputum and endotracheal aspirate specimens meeting high-quality criteria (≤10 epithelial cells/low power field [LPF] and ≥25 white blood cells/LPF) were included [1]. Patients also had nasopharyngeal and oropharyngeal (NP/OP) swabs collected and tested at the study sites using polymerase chain reaction (PCR) for a range of viral and atypical pathogens. Serotyping of isolated *Streptococcus pneumoniae* was performed at the CDC by Quellung reaction or PCR. Procalcitonin levels were also measured in available residual serum specimens [19, 20]. The study protocol was approved by the institutional review boards from the CDC and participating sites.

Urine Specimens

Stored (frozen) residual urine specimens from study biobanks in both Chicago and Nashville were identified. As previous studies have demonstrated that early in-hospital vaccination with the 23-valent pneumococcal polysaccharide vaccine (PPSV23) could interfere with SSUAD determinations [21], specimens collected after in-hospital vaccination were excluded, and when multiple specimens were available, only results from the earliest set of urine specimens were included.

SSUAD Testing

SSUAD testing of residual urine specimens was completed at Pfizer's Vaccines Research and Development Laboratory (Pearl River, New York). Testing was conducted blinded to all clinical information. Because each serotype assay was performed independently, multiple positive detections were possible [7–9]. Given that previous studies have documented the possibility of concurrent detection of 2 *S. pneumoniae* serotypes in blood cultures of patients with pneumococcal infections [22–24], it was prespecified per the testing laboratory protocol that codetections of up to 2 serotypes constitute a valid result and were reported. Detection of ≥3 serotypes, however, was classified as indeterminate [7–10].

Prior to the testing of EPIC study specimens, there was a necessary change in a critical assay reagent. It was determined that due to this reagent change, a reevaluation of the assay's positivity cutoff values was required. The positivity cutoff values were reevaluated with similar procedures and statistical parameters previously used for the validation of the SSUAD assays [9] and it was found that adjustments to the positivity cutoff value were required for serotypes 5, 14, and 23F (Supplementary Table 1). The revised positivity cutoff values were used to analyze the SSUAD results from the EPIC study specimens.

Statistical Analysis

To assess whether pneumococcal pneumonias were missed by traditional diagnostic testing (defined as blood cultures, BinaxNOW urine antigen detection [targets C-polysaccharide present in all pneumococcal serotypes], and high-quality respiratory specimen cultures), we determined the prevalence of pneumococcal detections with and without SSUAD assays; we also estimated the additional diagnostic yield from SSUAD assays, as well as their sensitivity and specificity relative to available serotyping information from pneumococcal isolates.

Previous studies have described clinical and illness severity differences between bacteremic and nonbacteremic pneumococcal pneumonias [25–27]. To compare clinical characteristics among patients with pneumococci detected by different detection modalities, we focused only on the subset of patients who had blood cultures, BinaxNOW urinary antigen detection tests, and SSUAD results available. We compared relevant clinical, radiological, and laboratorial characteristics among mutually exclusive groups of patients identified by different test results or combination of test results.

To explore potential early indirect protection derived from the change in childhood vaccination from PCV7 to PCV13 (initiated in the United States in early 2010) [17], we estimated changes in the proportion of pneumococcal pneumonia caused solely by the 6 serotypes included in PCV13 (1, 3, 5, 6A, 7F,

and 19A), but not in PCV7 (4, 6B, 9V, 14, 18C, 19F, and 23F) over time. Since the EPIC study enrolled patients from January 2010 through June 2012, we compared detections between 2 consecutive July–June periods (2010–2011 and 2011–2012) to account for adequate time to implement routine PCV13 immunization and for seasonal variability. We used a multivariable logistic regression model to compare the proportion of specific pneumococcal detections across those periods, while accounting for relevant covariates measured in the EPIC study: age (in years), gender, presence of chronic comorbidities, and exposure to young children (<5 years old) [1]. These young children generally represent the major reservoir, and an important source of transmission of *S. pneumoniae* for their close contacts [17, 28, 29]. Categorical variables were compared using χ^2 or Fisher exact tests, as appropriate, while continuous variables were compared using Kruskal-Wallis tests. A P value < .05 was considered significant. Statistical analyses were conducted using Stata version 14.3 software (StataCorp, College Station, Texas)

RESULTS

Estimation of Disease Burden and Contribution of SSUAD Detections to the Identification of Pneumococcal Pneumonia

Of 2320 adults hospitalized with radiographically confirmed pneumonia [1], 1901 (82%) had stored residual urine specimens available and were tested by SSUAD assays. No systematic differences were found in age or demographics between patients with and without urine specimens tested by SSUAD assays. However, patients without residual specimens available for SSUAD testing were more likely to have history of chronic kidney disease, seizures, higher confusion, uremia, respiratory rate, blood pressure, age ≥65 years (CURB-65) scores, and elevated procalcitonin levels (Supplementary Table 2). Some patients had indeterminate SSUAD results or urine specimens collected after in-hospital PPSV23 administration, or did not have any traditional pneumococcal tests done. After we excluded such patients, 1736 (75% of 2320) patients with SSUAD results and at least 1 traditional pneumococcal test were included in the assessment of pneumococcal pneumonia prevalence (Figure 1). Among these patients, 169 (9.7%) had pneumococcus detected by any method. Traditional diagnostics detected 93 (5.4%) pneumococcal cases, whereas SSUAD assays detected 110 (6.3%). Of the SSUAD-positive cases, 34 also had a positive traditional pneumococcal test and 76 were only positive by SSUAD assays. Thus, the addition of SSUAD to traditional testing increased the detection of pneumococcal cases from 93 to 169, an 82% relative increase.

The most common SSUAD-detected serotypes were 19A, 3, and 7F, accounting for 85 (77%) of all SSUAD detections. Two patients had concurrent detections of 2 serotypes: 1 with serotypes 18C and 3, and 1 with 18C and 7F (Table 1). Pneumococcal serotype information from traditional testing was available for 33 patients; 19 of these isolates were non-PCV13 serotypes and 14 were PCV13 serotypes. Among the 19 non-PCV13 serotypes detected by traditional methods, 18 tested negative by SSUAD assays (specificity 95%). The only exception was a 6C isolate that was identified by SSUAD assays as 6A. Among 14 PCV13

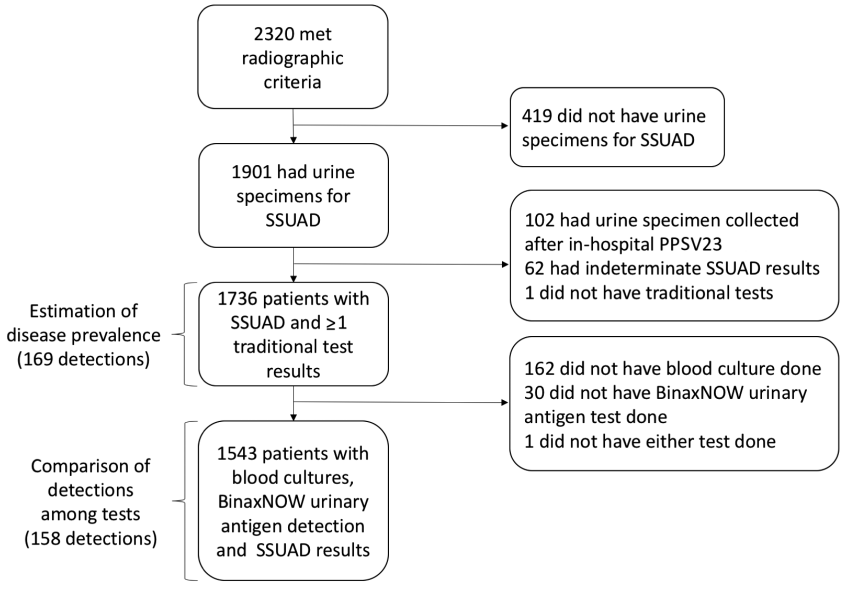

Figure 1. Study population. Traditional pneumococcal tests included blood cultures, BinaxNOW urinary antigen detection tests, and culture of respiratory specimens (high-quality sputum, bronchoalveolar lavage, pleural fluid, or endotracheal aspirates), as available. Serotype-specific urinary antigen detection indeterminate results included those with insufficient residual volume for testing, and those with >2 serotypes detected from the same urine specimens. Abbreviations: PPSV23, 23-valent pneumococcal polysaccharide vaccine; SSUAD, serotype-specific urinary antigen detection.

Table 1. Distribution of Pneumococcal Serotypes Identified by Traditional Tests and Serotype-Specific Urinary Antigen Detection Among 1736 Patients Hospitalized With Community-Acquired Pneumonia

Serotype[a]	Traditional Tests (n = 33), No. (%)	SSUAD (n = 110), No. (%)
19A (PCV13)	3 (9.1)	33 (30.0)
3 (PCV13)	6 (18.2)	28 (25.5)
7F (PCV13)	4 (12.1)	24 (21.8)
18C (PCV7)	0 (0)	8[b] (7.3)
6A (PCV13)	0 (0)	8 (7.3)
19F (PCV7)	0 (0)	2 (1.8)
5 (PCV13)	0 (0)	2 (1.8)
4 (PCV7)	1 (3.0)	2 (1.8)
23F (PCV7)	0 (0)	1 (0.9)
14 (PCV7)	0 (0)	1 (0.9)
1 (PCV13)	0 (0)	1 (0.9)
9V (PCV7)	0 (0)	0 (0)
6B (PCV7)	0 (0)	0 (0)
Non-PCV serotypes: 16F (4), 9N (3), 35B (2), 7C (3), 10A (1), 11A (1), 20 (1), 22F (1), 23A (1), 38 (1), 6C[c] (1)	19 (57.6)	0 (0)

Abbreviations: PCV7, 7-valent pneumococcal conjugate vaccine; PCV13, 13-valent pneumococcal conjugate vaccine; SSUAD, serotype-specific urinary antigen detection.

[a]PCV13 indicates a serotype included only in PCV13; PCV7 indicates a serotype included only in PCV7.

[b]Includes 2 codetections, 1 with serotype 3, and 1 with 7F.

[c]Identified as 6A by SSUAD. Data did not include a case with a positive SSUAD 19A detection who had a high-quality sputum sample (strain was serotyped as 19A) collected outside of the initial 72-hour threshold prespecified for the study.

isolates, SSUAD assays correctly detected and matched the serotype for all of them (sensitivity 100%).

Changes in the Prevalence of Pneumococcal Pneumonia due to PCV13 Serotypes Over Time

Of the 169 total cases with any positive pneumococcal test detected among 1736 patients, 110 (65% of all pneumococcal CAP) were caused by serotypes covered by PCV13, and the vast majority of those cases (87% [96 of 110]) were caused by serotypes exclusively covered by PCV13 but not included in PCV7. The proportions of pneumonia caused by the 6 pneumococcal serotypes exclusively covered by PCV13 during the first and second consecutive July–June study periods were 6.4% and 4.0%, respectively. After adjustment for age, gender, chronic comorbidities, and exposure to young children, the difference in the proportion of pneumonia caused by serotypes exclusively covered by PCV13 between the 2 periods was not statistically significant (odds ratio, 0.65 [95% confidence interval, .40–1.04]).

Comparison of Detections Among Tests

To compare the performance of the different diagnostic tests, we restricted our assessment to the 1543 patients enrolled in the EPIC study with blood cultures, BinaxNOW urinary antigen tests, and SSUAD assays determinations (Figure 1). In this subset, 158 (10.2%) patients had pneumococcal detections overall, including a total of 102 positive SSUAD detections, 61 positive BinaxNOW urinary antigen detection, and 32 positive blood cultures. Only 7 cases were detected by all 3 diagnostic tests, whereas 12 cases were only detected by blood culture, 34 were detected only by BinaxNOW urinary antigen detection, and 74 were detected only by SSUAD assays. Four pneumococcal cases were detected only by bronchoalveolar lavage or high-quality sputum cultures but with negative blood cultures, BinaxNOW urinary antigen tests, and SSUAD assays (Figure 2).

No major differences in patient characteristics were found among patients with detections with the various tests (Table 2), except for the assessments of disease severity and admission serum levels of procalcitonin, which were highest among patients with positive blood cultures. Disease severity and procalcitonin levels did not differ between patients positive only by SSUAD assays or only positive by BinaxNOW urinary antigen testing. The median serum procalcitonin concentration among patients with pneumococcal pneumonia detected by the pneumococcal detection modalities was >0.25 ng/dL, a commonly used threshold for the identification of bacterial infections needing antibiotic therapy (Table 2) [30, 31].

DISCUSSION

In this multicenter study of US adults hospitalized with radiographically confirmed CAP, the use of SSUAD assays increased pneumococcal detections from 5.4% to 9.7%, a nearly 2-fold increase in the number of cases. Consistent with previous reports [25–27], cases with positive blood cultures tended to have more severe disease and higher values of serum procalcitonin than those with culture negative pneumococcal pneumonia. Otherwise, no major differences in clinical

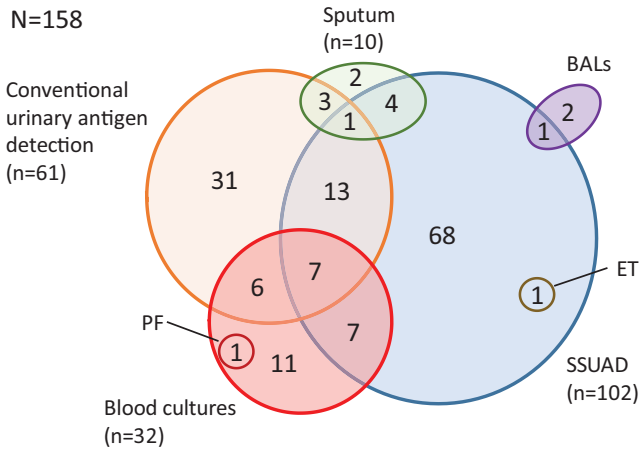

Figure 2. Comparison of detections among tests. The figure illustrates the distribution of pneumococcal detections among 1543 adults hospitalized with community-acquired pneumonia who had blood cultures, BinaxNOW urinary antigen detection tests, and serotype-specific urinary antigen detection testing performed. N indicates the total number of pneumococcal detections. Abbreviations: BAL, bronchoalveolar lavage; ET, endotracheal aspirate; PF, pleural fluid; SSUAD, serotype-specific urinary antigen detection assays.

Table 2. Clinical Characteristics of Patients With Pneumococcal Pneumonia, by Diagnostic Test Positive for *Streptococcus pneumoniae*

Characteristic	Blood Culture Positive Regardless of Other Results (n = 32)	BinaxNOW Urinary Antigen Test Only (n = 31)	SSUAD Only (n = 68)	BinaxNOW Urinary Antigen Test and SSUAD Only (n = 13)	Other Cultures[a] (n = 14)	*P* Value[b]
Demographics						
Age, y, median (IQR)	50.5 (39.5–66.0)	61.0 (47.0–72.0)	57.5 (43.5–66.0)	59.0 (52.0–75.0)	56.0 (51.0–63.0)	.38
Male sex	20 (63)	9 (29)	31 (46)	5 (38)	9 (64)	.056
White race	20 (63)	14 (45)	32 (47)	9 (69)	7 (50)	.567
Hispanic ethnicity	5 (16)	6 (19)	7 (10)	1 (8)	1 (7)	.56
Medical history						
Asthma	3 (9)	4 (13)	13 (19)	1 (8)	1 (7)	.55
Use oxygen at home	0 (0)	2 (6)	0 (0)	0 (0)	2 (14)	.013
Heart failure	2 (6)	9 (29)	8 (12)	1 (8)	2 (14)	.086
Diabetes mellitus	5 (16)	8 (26)	15 (22)	1 (8)	4 (29)	.57
Chronic kidney disease	3 (9)	3 (10)	4 (6)	3 (23)	4 (29)	.076
On dialysis	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	.39
Chronic liver disease	4 (13)	0 (0)	3 (4)	0 (0)	0 (0)	.11
Immunosuppressive condition	1 (3)	3 (10)	0 (0)	1 (8)	1 (7)	.16
HIV	0 (0)	0 (0)	3 (4)	1 (8)	0 (0)	.36
Cancer (excludes skin cancer)	6 (19)	3 (10)	5 (7)	1 (8)	3 (21)	.35
Seizure	0 (0)	1 (3)	0 (0)	1 (8)	1 (7)	.16
Dementia	0 (0)	1 (3)	3 (4)	2 (15)	0 (0)	.15
Stroke	0 (0)	2 (6)	4 (6)	1 (8)	1 (7)	.69
Clinical characteristics at admission						
CXR consolidation	28 (88)	25 (81)	55 (81)	11 (85)	12 (86)	.93
CXR other infiltrate	5 (16)	7 (23)	18 (26)	3 (23)	5 (36)	.64
CXR pleural effusion	11 (34)	12 (39)	26 (38)	2 (15)	4 (29)	.56
Codetection of other pathogen	5 (16)	8 (26)	24 (35)	4 (31)	4 (29)	.37
CURB-65 score, median (IQR)	2.0 (1.0–2.0)	1.0 (0.0–2.0)	1.0 (0.0–1.0)	1.0 (0.0–3.0)	1.0 (0.0–2.0)	.079
PSI score, median (IQR)	97.5 (66.0–121.0)	71.0 (61.0–96.0)	67.5 (51.0–94.5)	73.0 (52.0–99.0)	86.0 (54.0–123.0)	.14
Procalcitonin, median (IQR)	7.8 (2.7–27.3)	0.3 (0.1–3.4)	0.6 (0.1–4.6)	3.1 (1.5–30.2)	2.8 (0.4–4.4)	<.001

Data are presented as No. (%) unless otherwise indicated. All groups are mutually exclusive.

Abbreviations: CURB-65, confusion, uremia, respiratory rate, blood pressure, age ≥65 years; CXR, chest radiograph; HIV, human immunodeficiency virus; IQR, interquartile range; PSI, Pneumonia Severity Index; SSUAD, serotype-specific urinary antigen detection assay.

[a]Cultures include bronchoalveolar lavage, pleural fluid, and high-quality sputum.

[b]*P* values correspond to comparisons across groups. When significant differences were detected across groups, pairwise comparisons were conducted between pneumococcal pneumonia cases detected by traditional urinary antigen tests and SSUAD. No significant differences were observed between those groups.

characteristics were observed among cases detected with the different diagnostic tests.

Enhanced detection of pneumococci in cases of CAP has been previously demonstrated with other nontraditional diagnostic techniques [32]. Using a TaqMan multiplex PCR assay on NP/OP swabs and high-quality sputum specimens from a subset of adults enrolled in the EPIC study, the detection of pneumococcus in sputum specimens alone increased detections from 22% to 27% [33]. In a separate study of selected adults hospitalized with CAP who provided respiratory specimens, multiplex PCR on any sputum or endotracheal aspirates (ie, not restricted to high-quality specimens) increased identification of bacterial pathogens from 39% to 87% [32]. Similarly, Rello et al reported that among 353 patients admitted with pneumonia to the emergency department in a Spanish hospital, quantitative whole blood PCR for *lytA* increased identification of pneumococcal pneumonia by 85%, compared with blood cultures [34]. Of note, although the SSUAD assays identified previously unrecognized pneumococcal cases in the EPIC study, the revised prevalence reported in this study is likely conservative [35], as none of the traditional diagnostic tests has perfect sensitivity, and SSUAD assays included only 13 of >90 recognized serotypes [36]. For example, considering that 14 of 32 (44%) pneumococcal cases confirmed by blood culture were detected by the PCV13 SSUAD assays (Figure 2), we could estimate that the total SSUAD detections would only account for 44% of all pneumococcal cases.

We examined pneumococcal detections among patients who had blood cultures, BinaxNOW urinary antigen detection tests, and SSUAD assays. Patients who tested negative by SSUAD assays but positive through BinaxNOW urinary antigen detection likely represented infections with serotypes not included in

the 13 SSUAD assays. In contrast, patients detected by SSUAD but missed by the BinaxNOW urinary antigen test may reflect the limited sensitivity of BinaxNOW. Similarly, some cases with positive blood cultures were also missed by the BinaxNOW urinary antigen test, likely due to its limited sensitivity. Importantly, although some cases with a positive blood culture were missed by SSUAD assays, when serotype information was available, all blood isolates of serotypes included in SSUAD assays were correctly identified, suggesting that bacteremic cases missed by SSUAD likely represented serotypes not covered by these assays.

The start of enrollment for the EPIC study closely coincided with the replacement of PCV7 with PCV13 in the childhood US vaccination program. The vast majority of adult pneumococcal CAP cases caused by PCV13 serotypes were due to serotypes exclusively covered by PCV13. Serotypes covered only by PCV7 represented a small proportion (~13%) of identified pneumococcal CAP, reflecting the effectiveness of the pediatric PCV7 vaccination program at reducing PCV7 serotype disease in all age groups through reduced transmission and indirect protection [37–39]. We explored the potential early changes in pneumococcal pneumonia caused by serotypes exclusively included in PCV13 among adults not previously vaccinated with PCV13. The proportion of pneumonia hospitalizations with detected serotypes exclusively covered by PCV13 were numerically lower in the latter period of observation, suggesting an early sign of indirect protection from the pediatric PCV13 program. However, this difference was not statistically significant, likely because the number of pneumococcal detections was small, limiting the power to detect a statistically significant decline. Given that this study used only data from the first 2 years following PCV13 introduction, additional studies of the contribution of specific serotypes to the burden of pneumococcal pneumonia are warranted. Of note, some studies have already documented significant declines in all-cause pneumonia hospitalizations among unvaccinated adults following introduction of PCV13 in the United States [14].

Our findings must be interpreted in light of several limitations. First, no gold standard test to determine pneumococcal etiology exists, making determination of the relative performance of available tests challenging [6, 9, 36, 40]. Second, some patients did not have all specimens collected or all pneumococcal detection tests performed [1]. Third, some patients with specimens available had to be excluded because in-hospital vaccination with polysaccharide vaccine may have influenced SSUAD pneumococcal detections [21]. Fourth, although SSUAD-positive results have been reported among otherwise healthy HIV-infected adults colonized with pneumococcus [40], we did not determine the frequency or impact of pneumococcal nasopharyngeal colonization on SSUAD results. Finally, our study focused on patients enrolled from 2 cities in 3 tertiary academic medical centers, 1 county-funded public hospital, and 1 academic community hospital, and our findings may not be directly applicable to other settings.

In summary, use of novel SSUAD assays nearly doubled the identification of pneumococcal pneumonia among adults hospitalized with CAP. Observations from the first 2 years after replacement of PCV7 with PCV13 in the US childhood vaccination program suggest that the contribution of vaccine serotypes may be decreasing among unvaccinated adults and warrant follow-up studies. At the current time, SSUAD testing is not commercially available, but the results of this study highlight the need for more sensitive diagnostic tools for determining the etiology of CAP in adults in clinical settings.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Disclaimer. Investigators from the Centers for Disease Control and Prevention (CDC) participated in the study as authors. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC, the National Institutes of Health (NIH), or the Department of Veterans Affairs.

Financial support. The EPIC study was funded by the Influenza Division in the National Center for Immunization and Respiratory Diseases at the CDC. Additional support was provided in part by the NIH through K23GM110469 (principal investigator [PI]: W. H. S.), K23AI104779 (PI: D. J. W.) and R01AG043471 (PI: C. G. G.). SSUAD testing was conducted by Pfizer Inc.

Potential conflicts of interest. R. G. W. reports grants from CDC; funds to conduct clinical research from bioMérieux, Pfizer, and Vertex Pharmaceuticals; and personal fees from bioMérieux and Visterra. E. J. A. reports funds to conduct clinical research from MedImmune and NovaVax; personal fees from AbbVie; and nonfinancial support from Roche. D. J. W. reports grants from CDC. K. M. E. reports grants from CDC and Novartis; and other from Novartis. W. H. S. reports grants from CDC; research support from Pfizer; and personal fees from BioFire Diagnostics, Venaxis, Abbott Point of Care, Cempra Pharmaceuticals, and Ferring Pharmaceuticals. C. G. G. reports serving as a consultant for Pfizer and Merck. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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